Evolution of Multiple Sclerosis Ring Lesions: a Serial Phase Imaging Study at 7T

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Introduction: Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease of the central nervous system. Inflammation associated with MS lesions attracts iron-rich macrophages and reduces axonal clearance of iron. Magnetic resonance imaging at 7 Tesla can produce high-resolution gradient-echo phase images of MS lesions that quantify the local field shifts sensitive to iron[1,2,3]. In particular, a subset of MS lesions visible with phase imaging shows a distinct peripheral ring, i.e., a dark rim at the edge of a lesion, a contrast pattern usually not seen on other image modalities. The underlying biological source of this contrast was presumed to originate from iron-rich macrophages concentrated at the lesion edge[1]. However, it is not clear whether such rings would disappear over time as macrophages are expected to leave the acute inflammatory-demyelinating area. The purpose of this serial *in vivo* 7T study was to follow the evolution of MS lesions showing a phase contrast ring for up to 2.5 years.

Methods and Subjects: Five relapsing-remitting MS patients (3F:2M; mean age=51y; disease duration=17y; EDSS=3.1) were serially scanned on a whole-body GE 7T scanner (GE Healthcare) equipped with an 8-channel receive phased array coil (Nova Medical). 2D oblique axial gradient-echo images were acquired at a spatial resolution of 195×260μm or 350×350μm with TE/TR of 12 to 15/250 milliseconds, flip angle of 20°, slice thickness of 2mm, matrix/field of view 1024×768/20cm or 512×512/18cm, 3 repetitions (number of excitations), and scan time of approximately 9 or 6.5 minutes. The magnitude and phase images were reconstructed using the method previously described[4]. In brief, the magnitude signal from each channel in the complex image volume was combined using a root-sum-of squares algorithm[5] to obtain a magnitude image, then all multichannel phase images were unwrapped using the PRELUDE algorithm[6] to generate a full range of phase images. The baseline magnitude and phase images from each patient were used as templates, and all following images were registered to the templates using in-house software based on VTK CISG registration toolkit[7].

Results: A total of five peripheral phase ring lesions were found from all patients. None showed gadolinium contrast enhancement on conventional imaging. The mean follow-up time was 21.8 months (ranging from 15-31 months). The Figure below shows representative examples from 3 different lesions followed from baseline to month 1, month 4 and month 15. None (0/5) of the peripheral phase ring lesions disappeared over time, even for the lesion followed for up to 31 months. Furthermore, none of them showed obvious qualitative variation of contrast intensity and/or morphology.

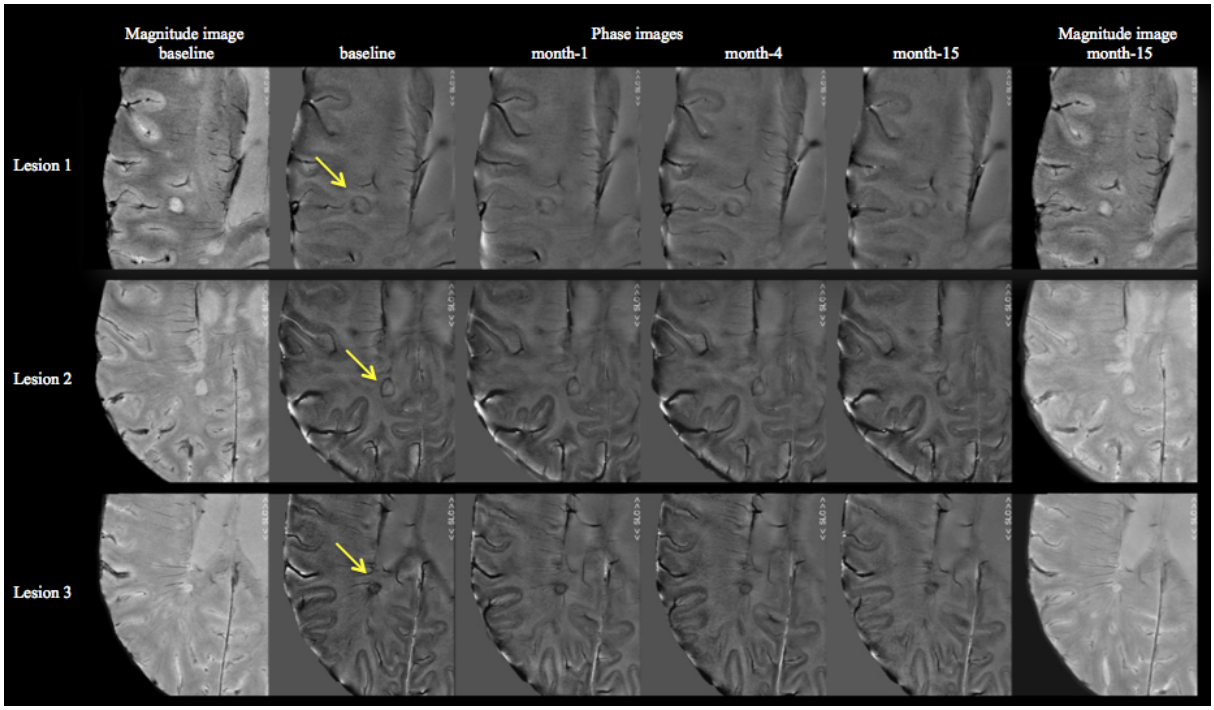

Figure. Evolution of three different peripheral phase ring MS lesions. From left to right, the phase images were acquired at baseline, month-1, month-4, and month-15. For comparison, T2*-weighted gradient-echo magnitude images at baseline and at the most recent time point are also shown. The yellow arrows show the location of the baseline phase ring lesion for each patient.

Discussion/Conclusion: The current data support the concept that once they have been formed, the peripheral rings in MS lesions that are observed using phase images remain stable with time. Although direct histopathological studies confirmed the presence of iron in microglial/macrohages cells in MS grey matter[8], additional histopathological work in white matter lesions is required to elucidate whether early iron-laden macrophages are leaving iron behind after clearance or, alternatively, the source of the phase signal is independent of these cells. Of interest is that we were able to use our image registration software to align serial 7T images from individual patients and make comparisons over extended time periods. Further work is underway to increase the sample size so that concrete statistical analysis can be performed.

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